REMARKS

Applicants have the following comments in support of this amendment.

Claim Amendments – Reference to Disclosure

Independent Claims 1 and 19 have been amended to be more explicitly directed to an embodiment of the present application, i.e. intracorporeal pharmaceutical compositions consisting of various formulations of certain halogenated xanthenes selected from a group consisting of:

- 4,5,6,7-Tetrabromoerythrosin,
- Monobromoerythrosin,
- Dibromoerythrosin,
- Tribromoerythrosin,
- Monochloroerythrosin,
- Dichloroerythrosin,
- Trichloroerythrosin,
- Monofluoroerythrosin,
- Difluoroerythrosin,
- Trifluoroerythrosin,
- 2',7'-Dichloro-4,5,6,7-Tetrafluorofluorescein,
- 2',4,5,6,7,7'-Hexafluorofluorescein, and
- 4,5,6,7-Tetrafluorofluorescein.

These halogenated xanthenes were previously the subject of dependent Claims 4 and 22 (now canceled in favor of the independent claims), and are enumerated in the specification of the present application at paragraph [0030].

In addition, independent Claims 1 and 19 have been amended to indicate that the claimed forms of the aforementioned halogenated xanthenes are disodium or dipotassium salts. Support for such amendment may be found, for example, in Table 1 of the present application, which illustrates that groups R^1 and R^2 of the halogenated xanthenes (see Figure 1a for the structural designation of these groups) may be, for example, sodium (Na) or potassium (K). This particular identity of the claimed forms of the halogenated xanthenes is further illustrated by Figure 1b, which shows an example of rose bengal in its dibasic form (i.e., as a disodium salt). Furthermore, Table 1 lists various dibasic salts of the halogentated xanthenes, including disodium 4,5,6,7-tetrabromoerythrosin.

Accordingly, Applicants respectfully submit that the amendments have not added any new matter, and the amendments to the claims are clearly supported by the application as filed. Therefore, it is requested that they be entered.

Finally, in order to advance the prosecution of this application Applicants have canceled Claims 3, 4, 21, and 22 without prejudice or disclaimer since such claims were rendered inconsistent or redundant as a result of the aforementioned amendments to independent Claims 1 and 19.

Novel Composition of Matter

Amended independent Claims 1 and 19 are directed to various pharmaceutical compositions that contain certain highly-halogenated halogenated xanthenes, including 4,5,6,7-Tetrabromo-erythrosin, none of which are believed to have been described in the prior art. Due to the relative

complexity of synthesis of such compounds and other factors, such as stability considerations, Applicants believe they have invented new compounds which represent a novel extension to the halogenated xanthene family. For example, Rose Bengal (which formerly comprised the most halogen-rich member of the halogenated xanthene family) has been known for over 100 years. Nonetheless, knowledge of its properties and those of the other previously known halogenated xanthenes (such as phloxine B, erythrosin, and eosin) has not led those skilled in the art to conceive, suggest, synthesize or investigate the currently claimed highly-halogenated halogenated xanthenes. Nor has anyone else conceived of pharmaceutical compositions consisting of halogenated xanthenes for any chemotherapeutic treatment of diseases prior to Applicants' work. Accordingly, Applicants respectfully submit that the claimed highly-halogenated halogenated xanthenes, and the various claimed pharmaceutical compositions containing such highly-halogenated halogenated xanthenes, of the claims of the present application are novel over the prior art.

Applicants will now address each of the Examiner's comments and rejections in the order in which they appear in the Office Action.

Claim Rejections – 35 USC §102

Rejection over Williams

In the Office Action, the Examiner rejects Claims 1-3, 10, 19-22, and 27 under 35 U.S.C. §102(b) as being anticipated by Williams et al. (US 5,576,013). This rejection is respectfully traversed for at least the following reasons. As explained in more depth below, Williams does not disclose or suggest the claimed subject matter.

First, Williams does not disclose or suggest the claimed pharmaceutical compositions that contain certain highly-halogenated halogenated xanthenes, including 4,5,6,7-Tetrabromoerythrosin. Instead, the disclosure in Williams is limited to certain other types of compositions containing Rose Bengal as shown by the following passage:

> "*Photosensitizing agents* that can be used are those that will render blood in target tissues sensitive to coagulation from exposure to light. Exemplary agents and a few of the light frequencies to which they are sensitive *include ... rose bengal* (550 nm)...." [col. 5, lines 7-14 in Williams, emphasis added]

Thus, Williams is concerned with certain known *photosensitizing agents*, such as Rose Bengal, and their potential use in photocoagulation of neovasculature. There is no mention in Williams of the specific halogenated xanthenes of amended independent Claims 1 and 19. In fact, there is no disclosure whatsoever in Williams on the subject of any other halogenated xanthenes than Rose Bengal.

Second, as previously explained in Applicants' Amendment D, Williams' teachings require use of certain formulation features that are unnecessary (and in fact undesirable) with the presently claimed invention. For example, the compositions of Williams *require formulation with a penetrating solvent* or *in a gel, lotion, cream or ointment.* (col. 5, lines 50-51, emphasis added) To this end, Williams lists a large number of penetrating solvents necessary for enhancing penetration of his agent into tissue, including the following passage:[1]

> "Suitable penetrating solvents are solvents ... which will enhance percutaneous penetration of the [photosensitizing] compound. Solvents which

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[1] While the Examiner relies on the mention of "direct injection" at col. 5, ln. 35 and "injecting" in Claim 4 of Williams, there is nothing in the reference to suggest what formulation is allegedly injected into the tumor or that the formulation injected into the tumor is different than the only formulas discussed in the reference, under the heading "Topical Formulations" starting at col. 5, ln. 40 in Williams.

have this property include proparacaine, dimethyl sulfoxide, ..." [see col. 6, line 56 - col. 7, line 6]

Accordingly, Williams teaches away from an intracorporeal pharmaceutical composition consisting of a halogenated xanthene in an aqueous solution, as recited in independent Claim 1 of the present application, since such aqueous solutions do not incorporate the penetrating solvents in Williams' compositions.

Williams also teaches away from intracorporeal pharmaceutical compositions in delivery vehicles consisting of tablets, capsules or suppositories, as recited in amended independent Claim 19 of the present application. Instead, Williams teaches that photosensitizers, in order to be effective, must be formulated in a "gel, lotion, cream, or ointment"(see e.g. Williams, col. 5, lines 42-51). Such liquid compositions clearly are different from the claimed solid compositions (i.e., tablets, capsules or suppositories).

As the presently claimed formulations do not incorporate Williams' penetrating solvents, nor are they gels, lotions, creams, or ointments, Williams does not disclose or suggest such formulations and actually teaches away from them.

Third, the disclosure in Williams concerns only photocoagulative methods and compositions that function by converting applied light energy into localized heating (see, for instance, col. 5, lines 7-14 in Williams); such methods and compositions only function upon application of specific forms of light energy. In contrast, the claimed compositions of the present application are intrinsically chemotherapeutic, and designed to function without requirement of additional work or stimulus (such as application of light energy). Accordingly, Williams' methods and compositions are functionally and compositionally unrelated to the claimed compositions.

Therefore, for the above-stated reasons, Williams does not disclose or suggest the claimed intracorporeal pharmaceutical compositions of independent Claims 1 and 19. Further, Williams not only fails to teach or suggest, the formulations consisting of aqueous solutions, tablets, capsules or suppositories of independent Claims 1 and 19, but, in fact, Williams *teaches away* from such formulations by requiring compositions formulated "with a penetrating solvent or in a gel, lotion, cream or ointment." Accordingly, independent Claims 1 and 19, and those claims dependent thereupon, are patentable over Williams, and it is respectfully requested that this rejection be withdrawn.

Rejection over Goers

The Examiner also continues to reject Claims 1, 3-4, 19, and 21-22 under 35 U.S.C. 102(b) as being anticipated by Goers et al.[2] This rejection is also respectfully traversed. For at least the reasons discussed below, Goers does not disclose or suggest the amended claims of the present application.

In particular, Goers fails to disclose or suggest the claimed pharmaceutical compositions of independent Claims 1 and 19 that contain certain highly-halogenated halogenated xanthenes, including 4,5,6,7-Tetrabromoerythrosin. Instead, the disclosure in Goers is limited to certain other types of compositions containing antibody derivatives of Rose Bengal, Eosin and other unnamed xanthenes as stated in the following passage:

> "According to one embodiment of the present invention, photochemicals including photosensitizers and photothermolytic agents may be used as

[2]Claims 3-4 and 21-22 have been canceled, rendering the rejection of those claims moot.

> therapeutic agents. Efficient photosensitizers include, but are not limited to ... rose bengal, ... xanthenes, ... eosin ... and the like." (col. 20, lines 48-58)

Goers does not identify these other "xanthenes", nor provide give any disclosure or suggestion as to what these might be. Goers clearly provides no disclosure or suggestion that these might be the presently claimed highly-halogenated halogenated xanthenes (and cannot as they had yet been conceived by the present inventors). Accordingly, Goers fails to disclose or suggest a pharmaceutical composition consisting of the highly-halogenated halogenated xanthenes of amended independent Claims 1 and 19 of the present application.

Second, amended independent Claims 1 and 19 exclude the antibody conjugates of Goers, since the presently claimed compositions consist of specific dibasic halogenated xanthene salts (in aqueous solution or formulated in a delivery vehicle) and cannot, therefore, include antibody derivatives since such dibasic forms preclude attachment of other moieties, such as antibodies, as both sites for attachment are tied up with sodium or potassium ions. Goers' teachings are predicated on targeting of certain compositions based on antigen-antibody methods, and hence require the use of antibody conjugate agents. In contrast, the present invention is free of such complexity of targeting, and instead show that the claimed compositions function via the *intrinsic targeting properties of the halogenated xanthenes*. For example, the specification of the present application indicates the following concerning intrinsic targeting:

> "In general, the halogenated xanthenes are characterized by ... a *propensity for selective concentration or retention in certain tissues and cells*, a high cytotoxicity upon such concentration or retention, and by chemical and physical properties that are substantially unaffected by the local chemical environment or by the attachment of functional derivatives at positions R^1 and R^2. Such factors make these chemical agents, and in particular chemotherapeutic medicaments formulated from such agents, excellent for the treatment of disease in human and animal tissues." (paragraph [0027], emphasis added)

However, Goers teaches away from the compositions of the claimed invention by requiring complex antibody-based targeting (whereas the compositions of independent Claims 1 and 19 utilize the inherent propensity of the halogenated xanthenes to exhibit "selective concentration or retention in certain tissues"). Thus, the presently claimed invention is free of such complicated antibody-based targeting as taught in Goers.

Third, the antibody attachment method of Goers will interfere with the intrinsic targeting of the claimed dibasic salts of the halogenated xanthenes, thus undermining their potential for use as chemotherapeutic agents. For example, attachment of antibodies to the halogenated xanthenes is likely to adversely affect their solubility, thus significantly reducing their bioavailability for concentration or retention in diseased tissue. The following table provides aqueous solubility data for several halogenated xanthenes and their derivatives:

Compound	Solubility	Reference
Eosin	200 mg/mL (20%)	SIAL Handbook[3]
Ethyl Eosin	1 mg/mL (0.1%)	SIAL Handbook
Rose Bengal	100 mg/mL (10%)	SIAL Handbook
Rose Bengal Acetate	2.5×10^{-4} M (0.026%)	Bottiroli (1997)[4]

These data show that attachment of various moieties, such as ethyl groups and acetate groups, to dibasic halogenated xanthenes can dramatically reduce the solubility of the halogenated xanthene in physiologically relevant formulations, such as aqueous solution.

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[3] F.J. Green, The Sigma-Aldrich Handbook of Stains, Dyes and Indicators, Aldrich Chemical Company, Milwaukee, 1990. See pp. 304, 320, and 637. A copy of this reference is attached in the enclosed IDS.

[4] G. Bottiroli et al., "Enzyme-assisted cell photosensitization: a proposal for an efficient approach to tumor therapy and diagnosis. The rose bengal fluorogenic substrate." Photochem. Photobiol. 66(3) (1997) 374-383. A copy of this reference is attached in the enclosed IDS.

The antibody conjugates of Goers would have a similar reduction in solubility. Accordingly, conjugation of halogenated xanthenes with antibody tags, such as that taught by Goers, would render the claimed invention impossible and impractical due to the deleterious effects of such conjugation on agent solubility. Moreover, such conjugate agents, which would require very large quantities of antibody material in their synthesis, would be cost-prohibitive at chemotherapeutic dose.

Further, the conjugate agents of Goers fail to possess the same activity as the claimed compositions due to fundamental differences in their respective biological activity. The antibody targeting in Goers is predicated on recognition of antigenic material on the surface of tumors or tumor cells. Thus, this targeting functions by delivery of the conjugate agent to antigenic material located on the *outside of the cell* (note that since antibodies can't detect antigens present inside the cell membrane, the only location where they can interact with antigens is on the cell surface or outside of the cell). In contrast, Applicants have discovered that the claimed dibasic salts of the halogenated xanthenes function by *entering tumor cells*, whereupon they exhibit selective retention, in certain intracellular structures, at levels that precipitate death of such tumor cells. Thus, the inherent extracellular targeting of the conjugate agents of Goers renders such agents inappropriate for targeting intracellular structures, and clearly represents different biological activity relative to the presently claimed compositions. For at least this reason, the compounds disclosed in Goers would not possess the same activity as the claimed compositions.

Finally, as explained in depth in Amendments B and C, Goers does not describe the presently claimed chemotherapeutic pharmaceutical compositions, since commerce in such compositions in the U.S. would require specific labeling of such compositions regarding, among other features, indication and usage. Such labeling (i.e., chemotherapeutic compositions according to the claims

of the present application) would readily distinguish any such patented product from any product based on the teachings in Goers. For example, for the invention of Goers to be practiced as a pharmaceutical composition, it would require labeling for indication (i.e., as a photosensitizer) and use (i.e., apply product, then apply a specific wavelength and amount of light to cause product to work) that clearly distinguishes it from the claimed compositions (i.e., chemotherapeutic compositions where one just administers the product; unlike a photosensitizer, the product does not require additional light application in order to function). No user of such products would confuse the photosensitizer product of Goers and the chemotherapeutic product of the present application.

For at least the above-stated reasons, Goers does not disclose or suggest the presently claimed chemotherapeutic pharmaceutical compositions, consisting of disodium or dipotassium salts of the highly-halogenated halogenated xanthenes, and Goers actually teaches away from such compositions by requiring compositions comprising "antibody therapeutic agent conjugates." Accordingly, the claims of the present application are patentable over the cited reference, and it is respectfully requested that this rejection be withdrawn.

Rejection over Bottiroli

The Examiner also continues to reject Claims 1-4, 9-11, 19-22 and 27 under 35 U.S.C. 102(b) as being anticipated by Bottiroli et al.[5] This rejection is respectfully traversed, as Bottiroli does not disclose or suggest the amended claims.

First, Bottiroli fails to disclose or suggest the claimed pharmaceutical compositions that contain certain highly-halogenated halogenated xanthenes, including 4,5,6,7-Tetrabromoerythrosin.

[5] Claims 3-4 and 21-22 have been canceled, rendering the rejection of these claims moot.

Instead, the disclosure in Bottiroli is limited to certain other types of compositions containing, among other things, various xanthene derivatives:

> "Fluorogenic substrates in the present invention are derivates of xanthenes ... containing quencher groups such as for example the acetate, sulphate, phosphate, dibutyryl ester, galacto-pyranoside, glucoronide, acetamide-dioxyglucopyranoside groups, respectively recognisable by the enzymes: esterase, sulphatase, phosphatase, lipase, beta-galactosidase, beta-glucoronidase, and glucoso-aminidase." (col. 3, lines 16-24)

With the exception of Rose Bengal, Bottiroli does not identify any other xanthenes, nor give any suggestion of the claimed highly-halogenated halogenated xanthenes. Accordingly, Bottiroli fails to disclose or suggest the claimed pharmaceutical compositions with the recited highly-halogenated halogenated xanthenes.

Second, Bottiroli also requires conjugate agents that are chemically distinct and different from the claimed compositions of the present application and which are excluded by the claimed language. Bottiroli is unambiguous on this fact, for example, as illustrated by the following passage:

> "Fluorogenic substrates in the present invention are *derivates* of xanthenes ... *containing quencher groups*...." (p. 3, lines 22-24 in Bottiroli, emphasis added)

Thus, Bottiroli teaches that for any xanthene to have use in a pharmaceutical composition, it must be a specific derivative containing special fluorescence quencher groups. That Bottiroli teaches away from any non-derivative form of the xanthenes (such as the claimed disodium or dipotassium salts of independent Claims 1 and 19 of the present application) is clear since rose bengal acetate and any other of Bottiroli's fluorescence quencher conjugates are distinctly different compounds than the presently claimed dibasic halogenated xanthene salts.

Third, as described supra with regard to Goers, the conjugate agents of Bottiroli will not exhibit the intrinsic targeting of the presently claimed dibasic salts of the halogenated xanthenes,

thus undermining their potential for use as chemotherapeutic agents. For example, as described supra, the acetate derivative of Rose Bengal has a solubility of $2.5x10^{-4}$ M (0.026%) whereas the dibasic salt of Rose Bengal is soluble to concentrations of at least 10%. This enormous difference in solubility is attributable to changes in polarity of the molecule, as described by Bottiroli:

> "Rose bengal disodium salt is soluble in polar solvents.... Its low solubility in nonpolar solvents has been considered to limit somehow its possible applications in photodynamic therapy. At low concentrations, RB, as an anionic dye, is inhibited from entering the cells in the absence of a carrier....
>
> "To improve the applicability of the drug in photodynamic therapy, several hydrophobic RB derivatives have been developed that, because of their self-aggregation tendency, could be internalized by the cell directly...." (Bottiroli et al., ibid, p. 374)

Thus, by derivatizing the halogenated xanthenes, Bottiroli produces a non-polar conjugate that is very insoluble in aqueous environment. This process, as indicated by Bottiroli, changes the molecule from a polar molecule soluble primarily in polar environments to a non-polar molecule soluble primarily in non-polar environments. Moreover, such halogenated xanthenes must be delivered as polar, dibasic salts, as predicated by Claims 1 and 19. The non-polar conjugates of Bottiroli simply cannot exhibit the intrinsic targeting and chemotherapeutic effects of the presently claimed compositions. Thus, the non-polar conjugate agents of Bottiroli will not possess the anti-tumor chemotherapeutic activity of the claimed compositions.

Finally, as explained in depth in Amendments B and C, Bottiroli does not describe the presently claimed chemotherapeutic pharmaceutical compositions, since commerce in such compositions in the U.S. requires specific labeling regarding, among other features, indication and usage. As described supra with reference to Goers, the photosensitizers in Bottiroli are readily distinguishable from any product based on the teachings of the present application. No user of such

products would confuse the photosensitizer product in Bottiroli with any chemotherapeutic product of the present application.

For at least the above-stated reasons, Bottiroli does not disclose or suggest the claimed chemotherapeutic pharmaceutical compositions, consisting of disodium or dipotassium salts of the highly-halogentated halogenated xanthenes, and teaches away from such compositions by requiring compositions comprising " derivates of xanthenes ... containing quencher groups." Accordingly, the claims are patentable over this reference, and it is respectfully requested that this rejection be withdrawn.

Rejection over Schultz

The Examiner also continues to reject Claims 1, 3-4, 19, and 21-22 under 35 USC §102(b) as being anticipated by Schultz et al.[6] This rejection is respectfully traversed, as Schultz does not disclose or suggest the claims, as presently amended, for at least the following reasons.

First, Schultz fails to disclose or suggest the claimed pharmaceutical compositions that contain certain highly-halogenated halogenated xanthenes, including 4,5,6,7-Tetrabromoerythrosin. Instead, the disclosure in Schultz is limited to certain other types of compositions containing derivatives of other xanthenes, including Rose Bengal (col. 9, line 54 to col. 10, line 27). Schultz does not identify any other xanthenes, nor give any suggestion of the claimed highly-halogenated halogenated xanthenes. Accordingly, Schultz fails to disclose or suggest the pharmaceutical compositions consisting of the specifically recited highly-halogenated halogenated xanthenes of amended independent Claims 1 and 19.

[6] Claims 3-4 and 21-22 have been canceled, rendering the rejection of these claims moot.

Second, Schultz requires the use of conjugate agents, as illustrated by the abstract therein:

> "*Polypeptide compositions* are provided having a binding site specific for a particular target ligand and further *having an active functionality* proximate the binding site. The *active functionality may be a reporter molecule* .... Alternatively, the *active functionality may be a chemotherapeutic agent*, in which case the polypeptide compositions are useful for therapeutic treatment of various diseased states." (emphasis added)

Thus, the compositions in Schultz are conjugate compositions (containing either diagnostic or therapeutic agents, depending upon the type of "active functionality" attached to the polypeptide). In contrast, as described supra for the rejections over Goers and Bottiroli, independent Claims 1 and 19 of the present application, *exclude* such conjugate agents. Specifically, each independent claim clearly delineates that the sole active component consists of a disodium or dipotassium salt of a halogenated xanthene. Such dibasic salts are not conjugates of halogenated xanthenes. Accordingly, the agents in Schultz are not encompassed within the scope of the independent claims of the present application. Since the invention of the independent claims is free of the limitations required in Schultz and different than what is disclosed in Schultz, Schultz does not disclose or suggest the claimed invention.

Third, Schultz does not teach or suggest treatment of diseases with any halogenated xanthene. Instead, Schultz describes two separate categories of conjugated polypeptides, namely (a) diagnostic conjugate agents (i.e., "fluorescers") and (b) therapeutic conjugate agents. For example, Schultz states:

> "Novel polypeptides having binding sites capable of specifically binding a predetermined target ligand include at least one active functionality proximate the binding site.... *The active functionality may be a reporter molecule*, whereby the polypeptides will be *useful in detecting* the predetermined target ligand in a sample suspected of containing such ligand.... *Alternatively, the active functionality may be a chemotherapeutic agent*, whereby the polypeptide

will be *useful in treating a diseased state* by site-specific drug delivery." (col. 4, line 58 - col. 5, line 6, emphasis added)

Thus, the reporter-molecule conjugate (i.e., "fluoresecer") in Schultz is for *diagnostics* (i.e., "detecting the predetermined target ligand in a sample") while the chemotherapeutic-molecule conjugate is for *treatment*.

The respective identities of the two distinct classes are established by several passages therein, including the following:

> "*Reporter molecules* and compounds are selected to *provide a detectable signal .... Suitable reporter molecules include* chromogens (e.g., dyes and *fluorophores*)....
>
> "A wide variety of fluorescers may be employed either by themselves or in conjunction with quencher molecules. *Fluorescers of interest* fall into a variety of categories having certain primary functionalities. These primary functionalities *include ... xanthene*....
>
> "*Individual fluorescent compounds* which have functionalities for linking or which can be modified to incorporate such functionalities *include ... rose bengal*...." (col. 9, line 32 - col. 10, line 27, emphasis added in Schultz)

In this passage, Schultz teaches that the xanthenes comprise one of several classes of "fluorescers of interest," and rose bengal is listed as a specific *fluorescent compound* of interest. Thus, Schulz teaches that xanthenes are for *diagnostics* (i.e., as fluorescent diagnostic reporter molecules when conjugated to certain polypeptides), not treatment.

Schultz describes a separate class of chemotherapeutic agents, and teaches the following:

> "Chemotherapeutic agents will be selected depending on the diseased state which is being treated as well as on the nature of the target ligand.... Exemplary chemotherapeutic agents include toxins, toxin fragments, bactericides, radical scavengers, radical generators, alkylating agents, neurotransmitters, radionuclides, antiviral compounds, antifungal compounds, antineoplastic agents, antimycoplasmal agents, heavy metals, and the like. A list of suitable drugs is provided in Table 1. (col. 11, lines 8-21)

In contrast to the abovementioned case for "reporter molecules," Schultz fails to include xanthenes in this list of chemotherapeutic agents (this is also the case for Table 1 in the reference). Accordingly, despite reference to Rose Bengal for diagnostics, Schultz fails to disclose or suggest any pharmaceutical composition comprising a halogenated xanthene for therapeutic or chemotherapeutic treatment of disease and therefore fails to disclose or suggest the claimed chemotherapeutic pharmaceutical compositions of the present application.

Finally, as described supra with regard to Goers and Bottiroli, the conjugate agents of Schultz will not exhibit the same functional activity (i.e., intrinsic targeting and chemotherapeutic activity) as the claimed dibasic salts of the halogenated xanthenes. Schultz's conjugates will exhibit different solubility, polarity, and biological activity than the claimed compositions due to the attachment of polypeptide moieties onto the halogenated xanthene molecule. For example, Schultz's polypeptides will exhibit a very different affinity for cancer cells than that of the claimed dibasic salts of the halogenated xanthenes. It is highly unlikely that such conjugates could elicit an intrinsic chemotherapeutic effect. For at least these reasons, the polypeptide conjugate agents of Schultz will not possess the anti-tumor chemotherapeutic activity of the claimed compositions.

Thus, for at least the above-stated reasons, Schultz does not teach or suggest the claimed chemotherapeutic pharmaceutical compositions, consisting of disodium or dipotassium salts of the highly-halogenated halogenated xanthenes, but instead, teaches away from such compositions by requiring conjugates attached to "novel polypeptides." Accordingly, the claims of the present application are patentable thereover, and it is respectfully requested that this rejection be withdrawn.

For at least the above-stated reasons, it is respectfully submitted that each of the §102 rejections has been overcome, and it is requested that they be withdrawn.

Claim Rejections – 35 USC §103

Finally, the Examiner continues to reject Claims 2 and 20 under 35 U.S.C. 103(a) as being obvious over Goers et al.

While this rejection is respectfully traversed, since Claims 2 and 20 have been canceled, this rejection is moot. Therefore, it is respectfully requested that the §103 rejection be withdrawn.

Information Disclosure Statement

Applicants filed an information disclosure statement (IDS) on January 10, 2005 and are including an IDS herewith. It is respectfully requested that these IDSs be entered and considered prior to the issuance of any further action on this application.

Interview Request

If the Examiner still wishes to reject the claims of the present application after considering this amendment, then Applicants request an interview with the Examiner to discuss the rejections in further depth. Please contact the undersigned to set-up such an interview.

Conclusion

For at least the above-stated reasons, it is respectfully submitted that the claims of the present application are in an allowable form and are patentable over the cited references. Accordingly, it is requested that the application now be allowed.

If any fee should be due for this amendment, please charge our deposit account 50/1039.

Favorable reconsideration is earnestly solicited.

Respectfully submitted,

Date: May 18, 2005

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